An Investigation of the Effect of Mephenesin Carbamate (Tolseram) on Normal Hearing Thresholds as Determined by the Conditioned Psychogalvanic Skin Response and Conventional Pure Tone Audiometry

By

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INTRODUCTION

Statement of Purpose

The purpose of this investigation is to study the effects of mephenesin carbamate (Tolseram) on normal hearing thresholds as determined by two methods: the conditioned psychogalvanic skin response and conventional pure tone audiometry. A knowledge of these effects would assist in the evaluation of the efficacy of the utilization of this type of drug as a sedative-muscle relaxant during hearing testing.

Rationale

With the development and improvement of the pure tone audiometer has come an increasingly more reliable hearing test technique for evaluating the auditory acuity of the hard-of-hearing adult. At the same time, the inadequateness and unreliability of this means of testing the hearing of infants, children, malingerers and individuals with psychogenic deafness has been acknowledged. Many

audiologists, pediatricians, and otologists consider the subjective responses of children five years of age and under as unreliable.[1] While Westlake considers the responses of three and four year-old children as reasonably accurate,[2] Goldstein and co-workers point out that children as old as seven may present some difficulty in testing,[3] and Bunch believes that seven or eight year olds yield results which are only "approximately correct."[4]

The principal weakness of the conventional audiometric technique for young children lies in its dependency upon purely subjective responses and the conscious cooperation of the child. Frequently, he cannot be made to understand or comprehend what he is supposed to do. This is especially true if the child has a language problem. It is apparent, moreover, that pure tones tend to be meaningless, uninteresting, and unstimulating to the young child. His

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[1]John E. Bordley and William G. Hardy, "A Study in Objective Audiometry with the Use of a Psychogalvanic Response," _The Annals of Otology, Rhinology and Laryngology_, LVIII (September, 1949), 751.

[2]Harold Westlake, "Hearing Acuity in Young Children," _The Journal of Speech Disorders_, VII (March, 1942), 14.

[3]Robert Goldstein, _et al_., "Difficulty in Conditioning Electrodermal Responses to Tone in Normally Hearing Children," _The Journal of Speech and Hearing Disorders_, XX (March, 1955), 30.

[4]C. C. Bunch, _Clinical Audiometry_ (St. Louis: C. V. Mosby and Company, 1943), 48.

attention span is short. Having him sit perfectly still for as long as half an hour with the expectancy of achieving accurate results verges on the realm of the impossible.[5] Furthermore, the need has been recognized for a reliable means of testing and treating children younger than five years of age in order to discover as early as possible whether a hearing loss is present. An early differential diagnosis would facilitate the giving of prompt attention to securing a better social adjustment and training of the individual. As Myklebust points out, a child with a hearing loss who is incorrectly diagnosed and then treated as mentally deficient, aphasic or emotionally disturbed, or who is not diagnosed at all, will suffer. He will suffer not only from his deafness but also from being misunderstood. A prompt and accurate differential diagnosis followed by appropriate therapy will prevent this and also minimize some of the consequent psychological and personality effects of auditory impairment.[6] In addition, as a result of early diagnosis, therapeutic and remedial measures might be introduced at a period of life when the child is most amenable and responsive to such corrective measures and rehabilitative

[5]Jacqueline Keaster, "Quantitative Hearing Tests for Young Children," The Volta Review, L (September, 1948), 465.

[6]Helmer R. Myklebust, Auditory Disorders in Children (New York: Grune and Stratton, 1954), 1.

procedures. It is evident, especially when considering the fact that children having different types of auditory problems vary greatly in their needs, that if their full potentialities are not to be lost, an early and accurate differential diagnosis should be made.[7]

The need for testing young children, as well as others who cannot or will not give reliable audiograms by the finger-raising technique, has resulted in the attempt to develop new hearing tests which are more objective in nature than this conventional method. The new tests are ones in which conventional audiometry is expanded instead of replaced. Auditory stimuli of known frequency and intensity are used for an adequate analysis of the hearing spectrum rather than a dichotomous determination of hearing or not hearing,[8] as is sometimes achieved by close observation of the child as he is bombarded suddenly with various acoustical stimuli or in the otologist's examination of the ear through the tympanic membrane for movements of the stapedius muscle indicating cochlear activity.[9]

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[7]*Ibid*., 8.

[8]William G. Hardy and John E. Bordley, "Special Techniques in Testing the Hearing of Children," *The Journal of Speech and Hearing Disorders*, XVI (June, 1951), 122.

[9]H. G. Kobrak, "The Present State of Objective Hearing Tests," *The Annals of Otology, Rhinology and Laryngology*, LVII (December, 1948), 1018.

Michels and Randt, in 1947, recorded auditory stimuli with an electroencephalograph (EEG), but these stimuli were at high, supra-threshold intensity levels only. No attempt was made to measure hearing thresholds by this technique.[10] Further research is being conducted with the EEG by Chester Darrow of the Institute for Juvenile Research and by others.[11]

Responses which were more objective than those obtained with conventional pure tone audiometry were recorded at threshold intensity levels when the conditioned psychogalvanic skin reflex was applied to acoustic stimuli. Commonly called "PGSR" or "GSR" audiometry,[12] the principle behind the technique is relatively simple. Kenneth Stewart summarized it briefly as follows:

> . . . if a unidirectional current, a galvanometer, and the palmar regions of a human subject are connected as a simple series electric circuit, various galvanometer current-time relations will be observed. The changes in current with time, are caused by changes in skin resistance. The exact mechanism responsible for the resistance change is unknown.[13]

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[10]Bordley and Hardy, "A Study in Objective Audiometry with the Use of a Psychogalvanic Response," _loc. cit._, 751.

[11]Chester W. Darrow, "The Relation of Cerebral to Autonomic Activity in the Conditioned Emotional Reactions of Children," _The Annals of the New York Academy of Science_, LVI (February, 1953), 289-301.

[12]Also known as the Electrodermal Response (EDR).

[13]Kenneth C. Stewart, "A New Instrument for Detecting the Galvanic Skin Response," _The Journal of Speech and Hearing Disorders_, XIX (June, 1954), 169.

The changes in skin resistance in response to acoustic stimuli are used to indicate hearing acuity. A pure tone (conditioned stimulus--CS) is presented to the subject and is followed by a slight electric shock (unconditioned stimulus--UCS). The electric shock results in a change in skin resistance. With repetition of this cycle, conditioning occurs and the change in skin resistance (now the conditioned response--CR) will occur when the tone alone is presented and the shock is omitted. Thus, the response indicates that the subject heard the tone. As to whether or not the tone must be perceived in the consciousness of the individual in order to yield such a response or whether it may result from a synapse below the cortical level is not fully known. Experimental evidence is wanting in this area.

The proper administration and interpretation of PGSR audiometry can be extremely difficult. It requires a skilled specialist for operation of the equipment and an assistant for the equally delicate task of preparing and handling the child during the procedure. The test, to be effective, should be conducted under ideal conditions in a room with a low ambient noise level. The procedure requires that the conditions of the testing situation be controlled with great care.[14]

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[14]William G. Hardy and Miriam D. Pauls, "The Test Situation in PGSR Audiometry," The Journal of Speech and Hearing Disorders, XVII (March, 1952), 13.

The testing of children by means of PGSR audiometry, even when taking all possible precautions, offers special difficulties. Although it does not rely upon the subject's voluntary response to the tone, it is hampered by the difficulty which one may have in differentiating responses to other stimuli.[15] It is for this reason that the objectivity of PGSR audiometry has been questioned.[16] Naturally, a great deal of this depends upon the skill of the audiologist. Unless highly trained, there may be some uncertainty in distinguishing the PGSR's resulting from the acoustic stimuli from the PGSR's following other stimuli.[17] However, if highly skilled, the audiologist usually is able to distinguish the responses with a high degree of significance.[18]

The PGSR may be triggered by many stimuli--both internal and external. Such things as limb and body movements; deep breaths (motor responses); emotional thought

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[15]F. Thomas Galloway and Robert A. Butler, "Conditioned Eyelid Response to Tone as an Objective Test of Hearing," _The Journal of Speech and Hearing Disorders_, XXI (March, 1956), 47.

[16]Kenneth C. Stewart, "Some Basic Considerations in Applying the GSR Technique to the Measurement of Auditory Sensitivity," _The Journal of Speech and Hearing Disorders_, XIX (June, 1954), 174.

[17]_Ibid_.

[18]_Ibid_., 183.

processes; startle reactions; tactile, visual, and acoustic stimuli may cause a galvanic skin response or fluctuations in the galvanic readings.[19] Still other conditions may cause variation or interference with accurate interpretation. They include items such as the instrumentation, type and placement of electrodes and the kind, quality and amount of electrode jelly.[20] Under fairly well-controlled conditions with an experienced experimenter using the proper equipment, most of these extraneous stimuli may be controlled. However, limb and body movements may prove to be particularly troublesome.[21]

Accurate interpretation of responses is even more difficult with children who have additional problems such as cerebral palsy, athetosis, petit mal or some other type of cerebral degeneration or dysfunction.[22] Especially in these cases, any excessive movement on the part of the child will register as a change in the skin resistance level and easily be confused with the conditioned response which is sought. A high degree of motor involvement in a patient may produce such erratic movement of the galvanometer as to

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[19] Ibid., 174.

[20] Ibid.

[21] Hardy and Pauls, "The Test Situation in PGSR Audiometry," loc. cit., 13.

[22] Ibid., 23.

render testing with the PGSR virtually impossible. Even with less severe involvement, a discernible conditioned PGSR and a reliable estimate of the child's hearing acuity may be extremely difficult to obtain. In some instances, the mere lack of co-operation on the part of the child may render the test useless.

A means of controlling hyperkinetic, or at times just normal, juvenile activity would prove of great assistance to the clinical testing of young children by means of PGSR audiometry. Sedation and tranquilization might be a boon to the procedure and facilitate the testing of many children who are now denied the benefit of the test by the very nature of their pathological condition. A sedative, luminal (phenobarbital), has been suggested for use with very active, excitable children with hyperactive sympathetic nervous systems. This has not proved to be satisfactory.[23]

Medication is needed which will sedate and calm a child and also reduce any interfering motor activity, but not put him to sleep, reduce his hearing acuity or inhibit his conditioned galvanic skin responses. Because it involves hearing testing, the sedation must not, of course, in any way affect hearing thresholds particularly when they are determined by PGSR audiometry. The need for such a

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[23] Ibid.

sedative has been long recognized,[24] especially for very young children and infants since they can be uncommonly difficult to condition.[25]

In addition to rendering PGSR audiometry feasible for children who at present are prevented from benefiting from an objective hearing evaluation because of motor involvement, appropriate medication may be beneficial in testing normal children. By relaxing and tranquilizing them, the time taken to establish rapport and confidence may be reduced. This fact has recently been recognized by the psychiatrist in his use of the tranquilizing drugs when dealing with disturbed patients.[26] Concerning the very practical aspect of clinic administration, Hardy and Pauls point out that:

> An appropriate sedative that did not seriously interfere with PGSR responses would be a great boon in speeding the handling of a large clinical load.[27]

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[24] *Ibid*.

[25] Robert Goldstein, H. Ludwig, and R. F. Nauton, "Difficulty in Conditioning Galvanic Skin Responses: Its Possible Significance in Clinical Audiometry," *Acta Oto-Laryngologica*, XLIV (1954), 74.

[26] Louis S. Goodman and Alfred Gilman, *The Pharmacological Basis of Therapeutics* (New York: Macmillan, 1955), 1067.

[27] Hardy and Pauls, "The Test Situation in PGSR Audiometry," *loc. cit.*, 23.

It would seem that when some of the extraneous variables which affect PGSR audiometry are controlled, this method may open new horizons in the still relatively unexplored frontier of objective audiometry.

Historical and Background Material

Traditionally, the original studies of the phenomenon of conditioning have been attributed to the Russian scientist, Ivan Petrovich Pavlov. In 1902, however, at about the same time that Pavlov was studying the conditioning of salivary glands in dogs, an American physiologist, E. B. Twitmyer, also discovered the principle of conditioning, independently of Pavlov, while studying patellar reflexes. Keen interest in this so-called "higher mental process" led to further research in Russia under Pavlov and Bechterev and in the United States by Watson and others.[28]

Pavlov entertained the view that the "whole activity of the organism should conform to definite laws."[29] It was later recognized that the psychogalvanic skin response involves the whole organism. Cason succeeded in demonstrating, in 1922, that a human involuntary process, pupillary

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[28]Clyde E. Nobel, "Conditioned Generalization of the Galvanic Skin Response to a Subvocal Stimulus," The Journal of Experimental Psychology, LX (February, 1950), 16.

[29]Ivan Petrovich Pavlov, Lectures on Conditioned Reflexes (New York: International Publishers, 1941), 7.

dilatation and constriction, could be conditioned in the laboratory.[30] With the conditioning of myosis and mydriasis achieved, the conditioning of other involuntary processes was soon to follow and the road was paved for the conditioning of the Féré effect, later known as the psychogalvanic skin response.[31] Thus, it was found that the subtle autonomic changes in eccrine sweat gland activity might be conditioned as simply as salivation in the Pavlovian dog. New problems soon became evident however. It was discovered that a great variety of internal and external stimuli could evoke a galvanic skin response.

Actually, the psychogalvanic skin response was studied prior to the investigation of conditioning and independently of it. As early as 1879, Vigouroux's monograph on the diagnostic use of skin resistance appeared. Research on the PGSR was continued and carried on by such men as Féré, Tarchanov, Gildemeister, Jeffress, Darrow, Landis and Woodworth.[32] Credit for much of the work has

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[30]Hulsey Cason, "The Conditioned Pupillary Reaction," _The Journal of Experimental Psychology_, V (April, 1922), 108-146.

[31]F. Aveling, "The Conative Indications of the Psychogalvanic Phenomena," _Proceedings of the Eighth International Congress of Psychology_, VIII (1926), 228.

[32]Nobel, "Conditioned Generalization of the Galvanic Skin Response to a Subvocal Stimulus," _loc. cit._, 16.

been given to Féré who conducted extensive studies on the PGSR in 1888.[33]

In 1921, Golla first combined PGSR and conditioning and successfully established a conditioned psychogalvanic skin response.[34] Since that time, there have been numerous studies of the psychogalvanic skin response and conditioning by such men as Coombs, Culler, Grant, Haggard, Havland, Kimble and Littman.[35] It was not until recent years, however, with the work of Hardy, Bordley and Pauls, that the use of this technique to measure auditory acuity was developed as a clinical instrument.[36] Steadily, the application of the conditioned PGSR to audiometry has grown in popularity and reliability, with strong efforts to refine and improve upon the technique. Some authors, in fact, feel that the popularity of the PGSR audiometric technique now exceeds its reliability.[37] Stewart believes that the PGSR offers excellent opportunity for objective hearing measurement but

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[33]Stewart, "A New Instrument for Detecting the Galvanic Skin Response," loc. cit., 169.

[34]F. L. Golla, "The Objective Studies of the Neuroses: Lecture II," The Lancet, CCI (1921), 215-221.

[35]See Bibliography.

[36]Bordley and Hardy, "A Study in Objective Audiometry with the Use of a Psychogalvanic Response," loc. cit., 759.

[37]Stewart, "Some Basic Considerations in Applying the GSR Technique to the Measurement of Auditory Sensitivity," loc. cit., 182.

feels that ". . . much more work needs to be done before a truly objective measurement will be available to the practicing audiologist."[38]

One of the principal problems that needs to be solved concerns the application of PGSR audiometry to infants and young children. Although the technique offers some value in the clinical assessment of the hearing of adults, malingerers, or the psychologically deafened, its primary application is for young children. It may help to provide a means for an early differential diagnosis which is needed to effect a satisfactory adjustment for the individual child. Unfortunately, many children are difficult to condition. Furthermore, their normal active state or an abnormal hyperactive state, as in the case of neuropathy, will interfere with the correct interpretation of responses. With the activity and excessive movement controlled or reduced by a harmless sedative-muscle relaxant, PGSR audiometry, along with other more conventional techniques, may serve to confirm a differential clinical diagnosis and may help to distinguish language and communication disorders from peripheral deafness.[39]

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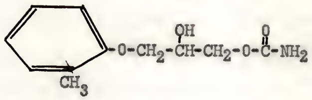
[38] Ibid.

[39] Goldstein, et. al., "Difficulty in Conditioning Galvanic Skin Responses: Its Possible Significance in Clinical Audiometry," loc. cit., 76.

Mephenesin Carbamate

Mephenesin carbamate (Tolseram),[40] a colorless, odorless, and tasteless white crystalline solid with a molecular weight of 225, is a carbamic acid ester of 3-(orthotoloxy)-1,2-propanediol with the structural formula:



Mephenesin carbamate is classified as an orally effective, centrally acting, skeletal muscle relaxant.[41] Producing muscular relaxation without concordant loss of consciousness, it has a tranquilizing or sedative effect.

The therapeutic use of muscle relaxants has become more popular in the last decade although as far back as 1910, Gilbert, Descomps, and Launoy observed that phenoxypropanediol, known in France as antodyne, caused reversible flaccid paralysis in animals.[42] Although the properties of

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[40] Tolseram is the trade name of mephenesin carbamate manufactured by E. R. Squibb and Sons, New York.

[41] Peter E. Dresel and Irwin H. Slater, "Observations on the Pharmacology of Mephenesin Carbamate," Proceedings of the Society for Experimental Biology and Medicine, LXXIX (February, 1952), 287.

[42] Goodman and Gilman, The Pharmacological Basis of Therapeutics, 206.

this compound and of other derivatives of the aromatic glycerol ethers were known for almost forty years, interest in muscle relaxants did not become keen until 1946 with the work of Berger and Bradley in Great Britain.[43] They were concerned with the parent drug of mephenesin carbamate, a compound known as Myanesin (mephenesin or Tolserol). Serving as a vital tool in experimental neurophysiology, mephenesin was first investigated as a possible adjunct to anesthesia. It later stimulated the search for a therapeutic agent which would be capable of abolishing abnormal muscle tone and eliminating involuntary movement without impairment of normal neuromuscular function.[44] Thus began the intensive study of muscle relaxants in order to find the means for alleviating spasticity, athetosis, dyskinesias, tremor, Parkinsonism, and similar neuromotor disturbances of central nervous system origin.[45] Skeletal muscular relaxation without loss of consciousness is mephenesin's main contribution. However, it has the disadvantages of toxic side-effects if given intravenously, and an extremely short duration of action, if any, when administered orally. The short and

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[43]Frank M. Berger and William Bradley, "The Pharmacological Properties of α,β-dihydroxy-γ-(2 methylphenoxy) propane (Myanesin)," The British Journal of Pharmacology, I (December, 1946), 265.

[44]Goodman and Gilman, The Pharmacological Basis of Therapeutics, 206.

[45]Ibid., 208-209.

transient nature of its action seriously limits the therapeutic usefulness of mephenesin.[46] The brief duration of action is explained by the fact that it is rapidly degraded metabolically by the liver to inactive acid forms such as β-(o-toloxy)-lactic acid and β-(2-methyl-4-hydroxy-phenoxy)-lactic acid.[47] Some method of preventing this rapid degradation might produce a long acting agent which could be administered in small, effective, non-toxic doses. A urea ester derivative of the parent compound, mephenesin carbamate was found to exhibit these properties. It was demonstrated to have a longer action than the old mephenesin as exemplified by mean paralyzing doses on white mice and by sustained blood levels. The prolongation of action, as might be expected, has been attributed to the fact that, unlike its predecessor, it has no terminal hydroxyl group, and therefore is not rapidly oxidized to the inactive β-toloxy lactic (myanesic) acid.[48]

The action of mephenesin carbamate is superficially similar to that of curare in that skeletal muscular relaxation occurs. Unlike curare, however, it causes a

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[46] Ibid., 208.

[47] Ibid.

[48] Dresel and Slater, "Observations on the Pharmacology of Mephenesin Carbamate," loc. cit., 287.

selective depression of the transmission of neural reflexes through the spinal cord rather than resulting in a blockage of acetylcholine at the myoneural junction. It particularly depresses transmission through the internuncial neurons.[49] The chief sites of action appear to be subcortical, in the brain stem, at the level of the thalamus and below in the spinal cord. Polysynaptic spinal reflexes appear to be more readily inhibited than monosynaptic reflexes, and supraspinal facilitation and suppression of these spinal reflexes are abolished.[50] As evidence against any cortical effects, clinical doses produce no detectable changes in the normal human electroencephalogram.[51]

Mephenesin carbamate is readily absorbed via the oral route but may be administered intravenously. It is quickly distributed uniformly throughout most of the body tissues. As a general rule, the concentration of the free drug in the plasma correlates directly with the pharmacological effects produced.[52]

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[49]Elwood Henneman, Arnold Kaplan and Klaus Unna, "A Neuropharmacological Study on the Effect of Myanesin (Tolserol) on Motor Systems," _The Journal of Pharmacology and Experimental Therapeutics_, XCVII (November, 1949), 340.

[50]Goodman and Gilman, _The Pharmacological Basis of Therapeutics_, 207.

[51]Henneman, _et. al._, "A Neuropharmacological Study on the Effect of Myanesin (Tolserol) on Motor Systems," _loc. cit._, 340.

[52]Goodman and Gilman, _The Pharmacological Basis of Therapeutics_, 207-208.

Mephenesin carbamate has been studied both in laboratory animals and in man. Mice and rats given oral doses of the drug ranging from 650 to 1,500 mgm. per kgm. weight daily for a period of thirteen weeks demonstrated no inhibition of growth, no hematological changes, or any significant pathology. Dogs receiving mephenesin carbamate for twenty-six weeks appeared normal with respect to growth, hematology, blood chemistry, and liver and kidney function. All organs were found to be normal at autopsy.[53]

Reports of toxicity following administration of the parent drug (mephenesin) indicated that any untoward reactions occurred only after massive doses were given intravenously over a long period of time. No such reactions resulted from the oral route of administration in which absorption is gradual.[54] The toxicity of mephenesin carbamate was found to be even less than that of mephenesin.[55] In

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[53]B. G. H. Thomas, J. W. Poutsiaka, J. S. Kulesza and C. R. Linegar, "Toxicity and Blood Level Studies on 3-(o-toloxy)-2-hydroxypropyl carbamate (Tolserol carbamate)," The Journal of Pharmacology and Experimental Therapeutics, CX (January, 1954), 48.

[54]Harold E. Godman and John Adriani, "Management of Patients with Tetanus; Some Clinical Experiences with Various Muscle-Relaxing Agents," The Journal of the American Medical Association, CXLI (November 12, 1949), 756.

[55]Thomas, et. al., "Toxicity and Blood Level Studies on 3-(o-toloxy)-2-hydroxypropyl carbamate (Tolserol carbamate)," loc. cit., 48.

view of the fact that no toxicity has been reported following the oral route for either mephenesin or mephenesin carbamate, the relative safety of the drug may be assumed, the likelihood of any untoward reactions being remote. There are no contraindications to the use of mephenesin carbamate.[56]

The fact that mephenesin carbamate is a safe, non-toxic, orally effective[57] sedative and muscle relaxant which does not affect the cranial nerves but whose site of action is at the level of the brain stem and below, might make it a likely candidate for pre-medication in PGSR and other types of audiometry where sedation is needed. However, before mephenesin carbamate, or similar agents with the same site of action, are employed, it would be desirable to investigate the effects of such medication upon hearing thresholds as determined by conventional audiometric methods as well as by PGSR audiometry. The latter aspect would indicate indirectly any possible effects of the drug on either conditioning or the psychogalvanic skin response. This would be especially desirable in view of the potential benefit that a medication such as mephenesin carbamate might

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[56] Ibid.

[57] A pleasant tasting peppermint suspension (Tolseram pediatric suspension) is available for young children.

offer in promoting the successful application of PGSR audiometry to infants and young children. Conversely, in the event that either hearing thresholds or the conditioned psychogalvanic skin responses are affected by such medication, the advisability of utilizing such a drug would be open to question. Should mephenesin carbamate not cause any statistically significant variation in hearing thresholds as determined by both of these methods, then further studies with mephenesin carbamate and similar preparations might be undertaken. These studies might then be designed to determine experimentally the feasibility of utilizing such medication in hearing evaluations of infants and young children, especially those with neuromotor disorders.

The purpose of the present study is to investigate the effects of mephenesin carbamate on normal adult hearing thresholds as determined by the conditioned PGSR and by conventional pure tone audiometry.

CHAPTER II

INSTRUMENTATION AND PROCEDURE

Statement of the Problem and Hypothesis

This study is an investigation of the effect of mephenesin carbamate (Tolseram) on normal hearing thresholds as determined both by conventional and PGSR pure tone audiometry. With the information obtained, an evaluation may be made of the feasibility of further investigation of the benefit of utilizing mephenesin carbamate and similarly acting drugs as a means of sedation and minimizing body movement in conjunction with clinical hearing testing of young children, particularly those with neurological disturbances.

The null hypothesis to be tested is that: There is no statistically significant difference between adult auditory thresholds after the administration of mephenesin carbamate or a lactose placebo whether tested by conventional pure tone audiometry or by conditioned PGSR audiometry. Any observed differences or discrepancies can be attributed to chance sampling variation of samples randomly drawn from the same population.

Instrumentation

The experimental portion of this study was conducted using the facilities of the Cleveland Hearing and Speech Center and Western Reserve University School of Medicine, Cleveland, Ohio.

The tests were administered in the basement level of the Cleveland Hearing and Speech Center in a sound-treated room with a low ambient noise level. This room was adjacent to a control room in which the equipment was placed. A large double plate glass window over the control panel in the control room looked out into the testing room. The subject could be observed directly through this window as well as through a mirror on the opposite wall of the testing room. (See Plates V, VI, and VII.)

In the testing room, the subjects were seated in a comfortable armchair, and the electrodes were applied to the proximal joints of the first and third fingers of each hand as well as on the wrist of the left hand. The finger electrodes were kept in place by means of adhesive tape and the wrist electrode by means of a rubber strap. A standard electrode jelly was used.[1] The faradic electric shock was received in the left third finger. The galvanic

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[1]Redux electrocardiographic electrode jelly.

skin response was picked up and measured from the right first and third fingers.

A wooden board designed to fit over the arms of the chair and extend as a table in front of the subject could be used with younger patients as a place on which to rest their arms and hands and place toys or similar distracting paraphernalia.[2] (See Plates V and VI.)

The wires from the electrodes and from the earphones ran into a panel on the wall of the testing room which was connected to the adjoining control room. Except for a hidden microphone and speaker, it was not deemed necessary or desirable to keep other equipment for the test in the testing room. A microphone, amplifier, and speaker, the audiometer, and the psychogalvanometer, with a recording device, were located in the control room.

A Grason-Stadler GS∆R automatic psychogalvanometer with a direct writing, heat stylus, Sanborn recorder plus a coupled Beltone 10-A audiometer were employed. Although the duration of and the interval between the conditioned (CS) and unconditioned (UCS) stimuli could be varied, once the CS was initiated, the CS and UCS were automatic and were electronically controlled. The duration of the CS and

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[2]With very young children, it is advisable to use electrodes which attach to the feet rather than to the hands or fingers.

UCS, as well as the interval between them, was kept constant throughout the experimentation.

The audiometer calibration was checked regularly at three week intervals with a standard 6 cc. coupler.[3] After preliminary testing, because of the excellence of the subjects' hearing and the low threshold values obtained, it was found necessary to add a 20 decibel (db) T-pad (12 ohm resistance) in the earphone line. Thus, the limit of the audiometer was extended from -10 db to -30 db. Since no subject was found to have a threshold value below -20 db at any frequency and most thresholds were considerably above this level, this pad proved to be very adequate. Both the conventional pure tone test and the PGSR evaluation were carried out using the same Beltone audiometer.

The Subjects

Twenty-four adult male subjects participated in this study. Their ages ranged from 21 to 28 years. The mean age was 23.79 years and the median age was 24. The distribution of ages was flat, showing bimodal peaks at 22 and 24 years of age. All the subjects were full-time medical students at Western Reserve University School of

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[3]Bruel and Kjaer Artificial Ear.

Medicine who, to their knowledge prior to testing, had normal hearing.

The subjects were selected at random from a group of 320 students at the Medical School. They were in good health at the time of the investigation. When selected, the subjects were aware of the fact that their hearing would be tested by two methods and that they would be given capsules to swallow prior to each of four tests. They knew that these capsules would contain either a muscle relaxant or a placebo. Having the subject cognizant of the possibility that he might be getting a placebo reduced the tendency toward over-reaction. For fear that he may be reacting to a placebo and therefore appear foolish, the subject tended to describe only real effects and symptoms, if any. The knowledge that a placebo is involved in the investigation may yield a more conservative type of introspection when subjectively judging the effects of the medication.[4]

Each subject received 2 grams of mephenesin carbamate or an equal amount of lactose placebo before each of the four tests. Both the drug and placebo were triturated and encapsulated so that no clues were available to the subject such as taste, color or odor. The dosage of 2 grams

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[4]Victor A. Drill (ed.), Pharmacology in Medicine (New York: McGraw-Hill Book Co., 1954), 34/10, 34/11.

(four 0.5 gram tablets) is within the limits of the usual recommended adult dose which ranges from 1.0 to 3.0 grams.[5] During the procedure, both the experimenter and the subjects were unaware of the capsules' contents. The administration of the medication was under the supervision of Valdemar M. Jordan, M.D., Assistant Clinical Professor of Otolaryngology, Western Reserve University School of Medicine.

Experimental Design

Each of the twenty-four subjects received four tests so that a total of ninety-six tests were administered in the study. The four tests that each subject was given were:

1. Conventional audiometry with Tolseram (CA-T)
2. Conventional audiometry with placebo (CA-P)
3. PGSR audiometry with Tolseram (PGSR-T)
4. PGSR audiometry with placebo (PGSR-P)

A counterbalanced order of tests was achieved by a Latin square arrangement.[6] The tests for each subject were administered one week apart at the same time of day, whenever possible, in order to reduce practice and fatigue effects which might not be cancelled by the counterbalanced order.

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[5]Goodman and Gilman, *The Pharmacological Basis of Therapeutics*, 208.

[6]Appendix Table 7. The initial order was selected from the random number tables appearing in Ronald A. Fisher and Frank Yates, *Statistical Tables for Biological, Agricultural and Medical Research*. (4th ed.; Edinburgh: Oliver and Boyd, 1953), 114.

Test Procedure

On each of the four testing periods, approximately one-half hour before the actual test was administered, the subject was given a sealed envelope containing four capsules. Thus, at the conclusion of testing, each subject had received a total of sixteen 0.5 gram capsules. On the outside of the envelope appeared the subject's number and the type of test he was to receive, whether conventional or PGSR audiometry. There were no other identifying marks or indications as to the contents of the envelope. The only way to ascertain what the contents were was to check on a master sheet. This was not done until all ninety-six tests had been administered.

The half-hour between the time of taking the capsules and commencing the tests allowed for maximum absorption of the drug and for peak plasma levels during the test.[7] All the capsules were swallowed with fruit juice in order to lessen the possibility of any gastrointestinal disturbances following the ingestion of Tolseram.[8]

During the half-hour waiting period, the subject was allowed to walk around, sit down, lie down, read, talk or

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[7]Dresel and Slater, "Observations on the Pharmacology of Mephenesin Carbamate," loc. cit., 287.

[8]E. R. Squibb and Sons, the manufacturer, suggest that Tolseram be taken after meals or with milk or fruit juice.

watch television. He was allowed to relax.[9] At the end of this time, the subject was seated in the testing room.

If he were to be tested by conventional pure tone audiometry, the subject was given the usual standard instructions for a pure tone threshold test. He was told to raise his finger as soon as he heard a tone and to keep his finger raised as long as he could hear the tone. The ear phones were placed on the subject and the test commenced with the experimenter observing the subject through the window in the control room.

The method of limits or just noticeable differences was employed. Serial explorations in intensity were made at each frequency using ascending and descending series. The intensity level which was the mean value of the tone first heard in the ascending series and the tone first missed in the descending series was called the threshold for that particular frequency. Only the right ear was tested in this investigation. It was assumed that the drug would affect both ears equally because the action of mephenesin carbamate is systemic rather than local.

Threshold values were obtained for 500, 1,000, 2,000, 4,000, and 8,000 cycles per second.

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[9]A lounge was available for this purpose.

If the subject were to be examined by PGSR audiometry, he would likewise be seated in the testing room one-half hour after taking the four capsules. The electrodes were applied with a liberal amount of electrode jelly to insure proper contact. The subject was told that all that he would be required to do for the test was to relax and sit quietly with as little body and limb motion as possible. He was informed that he would hear tones which might or might not be followed by a slight electric shock. There would be no overt response required of him. He was instructed not to speak during the test unless it was necessary. The subject was observed in the same manner as was used in the conventional type of audiometry, through the control room window and the mirror on the testing room wall. The control room was kept dark throughout the test so that the subject could not see through the window.

The subject was presented with a 1,000 cycle tone at an intensity of 40 db above the normal hearing threshold level (0 db). This initial unreinforced CS was given to determine the state of conditioning at the commencement of the test. The subject was then conditioned to this 1,000 cycle tone at an intensity level of 40 db. Although Doerfler and McClure found that a frequency of 500 cycles per second (cps) and an intensity level of 80 db were ideal for conditioning, they also showed that a 1,000 cps tone could

be used quite adequately. They conditioned their subjects to a 1,000 cycle tone at a level of 70 db above normal threshold.[10] In the present study, the subjects were conditioned to 1,000 cps because, in an evaluation of a patient's hearing, if extenuating circumstances permit only one frequency to be checked, it was felt that from the point of view of speech range the most desirable frequency to investigate would be 1,000 cps.

Stimuli, both CS and UCS, were presented according to a random schedule.[11] The time interval between successive tones was also varied randomly with a minimum of 20 seconds and a maximum of 90 seconds. These values are within the limits suggested by Stewart.[12]

Consistent with the findings of Hovland[13] and of

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[10] Leo G. Doerfler and Catherine T. McClure, "The Measurement of Hearing Loss in Adults by Galvanic Skin Response," _The Journal of Speech and Hearing Disorders_, XIX (June, 1954), 186.

[11] From the random number tables of Fisher and Yates, _Statistical Tables of Biological, Agricultural and Medical Research_, 114-119.

[12] Stewart, "Some Basic Considerations in Applying the GSR Technique to the Measurement of Auditory Sensitivity," _loc. cit._, 177.

[13] Carl I. Hovland, "The Generalization of Conditioned Responses: IV. The Effects of Varying Amounts of Reinforcement Upon the Degree of Generalization of Conditioned Responses," _The Journal of Experimental Psychology_, XXI (September, 1937), 261-276.

Meritser and Doerfler,[14] Doerfler and McClure found that resistance to extinction of the conditioned response is significantly greater with 40 to 60 per cent reinforcement than with 100 per cent reinforcement of the conditioned stimulus with the unconditioned stimulus.[15] In accordance with these findings, the subjects in this study were conditioned using partial (60 per cent) reinforcement.

Although no basis has been found for assuming that there is a difference between varied and constant intensity of stimuli as affecting the acquisition or extinction of the conditioned response,[16] the intensity level was kept constant at 40 db during the conditioning process of this investigation. The intensity level was varied only after the conditioned response was established and an estimate of the threshold was being made using the method of limits with ascending and descending series.

The tone (CS) was presented for 2.0 seconds duration. The shock (UCS) was given 0.5 second after the

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[14] Clay L. Meritser and Leo G. Doerfler, "The Conditioned Galvanic Skin Response Under Two Modes of Reinforcement," The Journal of Speech and Hearing Disorders, XIX (September, 1954), 356.

[15] Doerfler and McClure, "The Measurement of Hearing Loss in Adults by the Galvanic Skin Response," loc. cit., 186.

[16] Meritser and Doerfler, "The Conditioned Galvanic Skin Response Under Two Modes of Reinforcement," loc. cit., 357.

onset of the CS. The shock duration was 0.75 second and its intensity was varied from 0.15 milliamperes to 2.0 milliamperes, depending upon the individual subject's sensitivity and shock threshold. An attempt was made in each case to adjust the shock level to approximately three just noticeable differences (JND's) above the subject's threshold for the shock. The same shock intensity was used throughout the test for each subject.

Basal levels of skin resistance ranged from a low of 10,000 ohms to a high of 180,000 ohms. The mean value of the maximum resistance recorded on each subject was 61,670 ohms when Tolseram was administered and 63,750 when the placebo was given. The mean values of the minimum resistance were 43,130 ohms and 45,000 ohms with the administration of Tolseram and the placebo respectively. Differences in basal levels when the drug was given as compared with those measured when the placebo was used were not significant.

The criterion for conditioning was a minimum of three responses to three unreinforced tones. The total time required to establish conditioning ranged from 1 minute and 30 seconds to 1 hour and 10 minutes. In three tests, no conditioned responses were evident after 1 hour and 45 minutes. The attempt was abandoned after 150 trials. Two of the instances occurred with the same subject involving both his PGSR tests. It was not found possible to condition

him under the time restrictions of the experiment.

Each subject was presented with a 1,000 cycle 40 db tone which was reinforced randomly by shock 60 per cent of the time. When a conditioned response was obtained, the intensity level of the tone was gradually reduced in a descending series until a conditioned response no longer appeared. Then the tone intensity was gradually increased, in an ascending series, until the conditioned response appeared again indicating that the subject had heard the tone at that intensity. Thus, thresholds were determined by the method of limits as was done with conventional audiometry. Concerning the use of special criteria in considering responses, whenever possible, those used by Doerfler and McClure were followed. In their study, these criteria were evolved:

> An arbitrary decision was made to count three acceptable responses out of five presentations for a particular intensity level as indication that the subject heard the tone at that level. The lowest intensity level of presentation at which the subject responded with three Galvanic Skin Responses which met the criteria was accepted as threshold of hearing.[17]

As basic criteria for judging whether or not a deflection was a response, a minimum of 5 mm. in height and a 45° slope were used.[18]

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[17] Doerfler and McClure, "The Measurement of Hearing Loss in Adults by the Galvanic Skin Response," loc. cit., 187.

[18] Ibid.

After the threshold for 1,000 cps was established, a 2,000 cps tone was presented at 40 db. The method of limits was again repeated with occasional reinforcement when the responses became very low in amplitude. Just enough reinforcement was given to maintain conditioning. After the threshold value was ascertained for 2,000 cps, the process was repeated at 4,000, 8,000, and finally at 500 cps. A CS of 1,000 cps and 40 db (reference tone) was presented after each threshold value was obtained as a check on the level of conditioning. When necessary, reinforcing shocks were given.

Sufficient generalization occurred so that the initial conditioning process achieved with the 1,000 cycle 40 db tone was strong enough to carry over to the other frequencies and intensities. Consequently, the conditioned response to the 1,000 cycle tone was utilized to measure thresholds of frequencies up to 8,000 cps and down to 500 cps as well as intensity levels ranging from 40 db down to threshold levels for each frequency.

Little or no difficulty was encountered in distinguishing galvanic skin responses following the tone from random variations in skin resistance. The latter were very few in number as might be expected in testing co-operative adult subjects. This lack of difficulty in recognizing the PGSR is consistent with the literature.

Stewart found an extremely high degree of certainty in distinguishing conditioned PGSR's from responses to extraneous stimuli. He found less than one chance in a thousand of an error in distinguishing the PGSR from other responses.[19]

The test was terminated when thresholds were measured for each of the five frequencies. No attempt was made to do any experimental extinction of the conditioned response.

No instances of untoward reactions were experienced with the administration of either Tolseram or the lactose placebo in this experiment.

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[19]Stewart, "Some Basic Considerations in Applying the GSR Technique to the Measurement of Auditory Sensitivity," loc. cit., 180.

CHAPTER III

ANALYSIS AND EVALUATION OF THE DATA

Method Employed

To test the null hypothesis proposed in this study by an appropriate statistical method, an analysis of variance was used with two criteria of classification.[1] In the analysis, the variation between groups was compared to the variation within groups.

With variance analysis involving two criteria, there are actually three types of variation to be considered. There is the variation in the means of the rows (subject variation) and the variation in the means of the columns (test variation), as well as the variation in individual thresholds from an expected value of the combined test and subject effects.[2] This latter type of variation is presumably due to chance. Smith and Duncan refer to it as

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[1] George W. Snedecor, Statistical Methods (Ames: The Iowa State College Press, 1946), 253-317.

[2] James G. Smith and Acheson J. Duncan, Sampling Statistics and Applications (New York: McGraw-Hill Book Co., 1945), 429.

"'remainder' variation."[3] Utilizing these variations in the analysis, an estimate was made of the significance of the differences found between tests after the administration of mephenesin carbamate and after placebo administration, as well as differences between conventional and PGSR audiometry and differences among subjects.

Results

Mean threshold values obtained by the four tests at each of the five frequencies investigated appear in Table 1.

The results of the analysis of variance at each frequency, summarized in Tables 2 through 6, show that for 1,000, 4,000, and 8,000 cycles per second, there were no significant differences in thresholds, at the 5 per cent level of confidence,[4] after the administration of Tolseram or the lactose placebo as determined by PGSR and conventional pure tone audiometry. The F-Ratios obtained were 1.33 at 1,000 cps, 0.75 at 4,000 cps, and 0.69 at 8,000 cps.

For the frequencies 500 cps and 2,000 cps, the F-Ratios were calculated to be 3.17 and 3.28 respectively. Both of these values are significant at the 5 per cent level

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[3] *Ibid.*, 430

[4] An F-Ratio of 2.74 is significant at the 5 per cent level of confidence and an F-Ratio of 4.08 is significant at the 1 per cent level of confidence.

of confidence but were not significant at the 1 per cent level of confidence.

A statistical model having the characteristics of the population from which the samples in this study might be drawn was examined. The critical differences which would exist between subsamples at the 5 per cent and 1 per cent levels of confidence were determined.

The critical differences at 500 cps were calculated to be 1.38 at the 5 per cent level and 1.87 at the 1 per cent level of confidence. Those for 2,000 cps were found to be 1.43 at the 5 per cent level of confidence and 1.94 at the 1 per cent level of confidence. Only one of the differences between mean threshold values exceeded the critical difference at the 1 per cent level of confidence. The difference between the mean thresholds at 500 cps as determined by conventional audiometry and as determined by PGSR audiometry, both with placebo administration, was 1.88. Thus, it exceeded the critical difference at the 1 per cent level of confidence by 0.01.

At the 5 per cent level of confidence, mean threshold differences between conventional audiometry with placebo and PGSR audiometry with placebo exceeded the critical difference for both 500 and 2,000 cps.

Almost identical with the 1.88 difference in mean thresholds at 500 cps, the difference at 2,000 cps was 1.87.

However, these differences were in opposite directions. Thus, at 500 cps, the mean threshold value determined by conventional audiometry with placebo exceeded (in a negative direction) that measured by PGSR audiometry with placebo; whereas, at 2,000 cps, the converse was true. The mean PGSR audiometric threshold exceeded that determined by conventional audiometry. It is also interesting to note that the only significant differences occurred with the use of the placebo. There were no significant differences found between methods using Tolseram as compared with those using the placebo.

Since the differences in mean thresholds at 500 cps and 2,000 cps are actually contradictory, and since one might expect to obtain differences due to chance or random variation as large or larger in 5 times out of 100, these differences may not be significant. They might well be one of the 5 instances in 100 in which the differences are due to chance or sampling variation and random differences within the same population.

The F-Ratios for subject variation were significant at the 1 per cent level of confidence and beyond, at all of the five frequencies tested. This is consistent with the expected differences in thresholds among different subjects. Even though the subjects were somewhat homogeneous, that is, they were all normal hearing, male medical students with a

small range in age, there were significant differences in their auditory thresholds as measured in this study.

In the light of the above findings, the null hypothesis which states that there is no significant difference between adult auditory thresholds after the administration of mephenesin carbamate or a lactose placebo as tested by both conventional and PGSR audiometric techniques may not be rejected. Thus, mephenesin carbamate causes no statistically significant differences in hearing thresholds, whether they are measured by conventional or PGSR audiometry.

TABLE 1

MEAN THRESHOLD LEVELS IN DECIBELS

Test	Frequency (cycles per second)				
	500	1,000	2,000	4,000	8,000
CA-T	-10.00	-8.13	-7.08	-3.33	-0.42
CA-P	-10.21	-7.71	-6.88	-3.13	-1.25
PGSR-T	- 9.58	-8.13	-8.13	-3.96	-1.25
PGSR-P	- 8.33	-8.96	-8.75	-4.17	-0.42

TABLE 2

ANALYSIS OF VARIANCE FOR 500 CPS

Source	Sum of Squares	Degrees of Freedom	Variance Estimate	F-Ratio
Means of Columns (Tests)	50.79	3	16.93	3.17
Means of Rows (Subjects)	635.16	23	27.62	5.18
Error	367.96	69	5.33	
Total	1,053.91	95		

TABLE 3

ANALYSIS OF VARIANCE FOR 1,000 CPS

Source	Sum of Squares	Degrees of Freedom	Variance Estimate	F-Ratio
Means of Columns (Tests)	19.79	3	6.60	1.33
Means of Rows (Subjects)	586.46	23	25.50	5.13
Error	342.71	69	4.97	
Total	948.96	95		

TABLE 4

ANALYSIS OF VARIANCE FOR 2,000 CPS

Source	Sum of Squares	Degrees of Freedom	Variance Estimate	F-Ratio
Means of Columns (Tests)	56.25	3	18.75	3.28
Means of Rows (Subjects)	845.83	23	36.78	6.44
Error	393.75	69	5.71	
Total	1,295.83	95		

TABLE 5

ANALYSIS OF VARIANCE FOR 4,000 CPS

Source	Sum of Squares	Degrees of Freedom	Variance Estimate	F-Ratio
Means of Columns (Tests)	17.71	3	5.90	0.75
Means of Rows (Subjects)	4,612.46	23	200.54	25.45
Error	543.79	69	7.88	
Total	5,173.96	95		

TABLE 6

ANALYSIS OF VARIANCE FOR 8,000 CPS

Source	Sum of Squares	Degrees of Freedom	Variance Estimate	F-Ratio
Means of Columns (Tests)	16.66	3	5.55	0.69
Means of Rows (Subjects)	13,658.33	23	593.84	73.40
Error	558.34	69	8.09	
Total	14,233.33	95		

CHAPTER IV

SUMMARY AND CONCLUSIONS

In this experiment, twenty-four normal hearing, adult male subjects were tested in four ways using a Latin square counterbalanced order. Each subject's hearing thresholds at 500 cps, 1,000 cps, 2,000 cps, 4,000 cps, and 8,000 cps were estimated by conventional audiometry following the administration of mephenesin carbamate (Tolseram) or a lactose placebo, as well as by PGSR audiometry also following the administration of mephenesin carbamate or a suitable placebo. A statistical analysis of variance of the quantitative data led to the following conclusions:

1. Mephenesin carbamate has no statistically significant effect upon hearing thresholds as determined by PGSR audiometry.

2. Mephenesin carbamate has no statistically significant effect upon hearing thresholds as determined by conventional pure tone audiometry.

3. Differences in threshold as measured by either conventional pure tone or PGSR audiometry following the

administration of the placebo are probably due to chance.

4. There were no statistically significant differences found in hearing thresholds whether measured by conventional pure tone or PGSR audiometry.

In the light of these findings, it is recommended that further investigation be made into the feasibility of employing mephenesin carbamate, and similarly acting pharmaceutical preparations, as sedatives and tranquilizers during PGSR and other types of audiometry as the demand rises for facilitation of testing.

Since mephenesin carbamate may be used without interfering with or significantly affecting hearing thresholds, a way is paved for further inquiry as to the drug's effect in reducing the activity of normal children and the hyperactivity of patients with neuromotor disorders.

The eventual goal to be achieved is the selective administration of the drug, under proper medical supervision, as pre-medication in clinical audiometry. This will be especially applicable to the testing of those individuals whose problem makes a hearing evaluation necessary and vital for an early differential diagnosis, and whose problem also makes testing difficult or impossible without some means of reducing or removing interfering factors.

Thus, this study should prove to be a valuable contribution, from a heuristic point of view, in that it is hoped it will stimulate new investigations as to the practicability of utilizing muscle relaxants as a means of sedation in facilitating clinical audiometry involving patients whose hearing thresholds cannot be evaluated satisfactorily by existing methods.

APPENDICES

PLATE I

VIEW OF THE CONTROL ROOM

The experimenter operates all equipment and observes the subject from this room. On the far left is the Beltone Audiometer. The Grason-Stadler Psychogalvanometer with an interconnected recorder lies immediately to the right of the Audiometer. The microphone and amplifier are in the foreground below the window which offers a view of the testing room. Wires connecting the two rooms pass through the panel on the wall in the upper left-hand corner.

PLATE II

VIEW OF THE EQUIPMENT

The Beltone Audiometer on the left connects directly to the Grason-Stadler Psychogalvanometer and is controlled automatically by an electronic timing mechanism in the Psychogalvanometer. A microphone and earphones for intercommunication with the subject in the testing room are in the lower right-hand corner.

PLATE III

THE GRASON-STADLER GSΔR PSYCHOGALVANOMETER

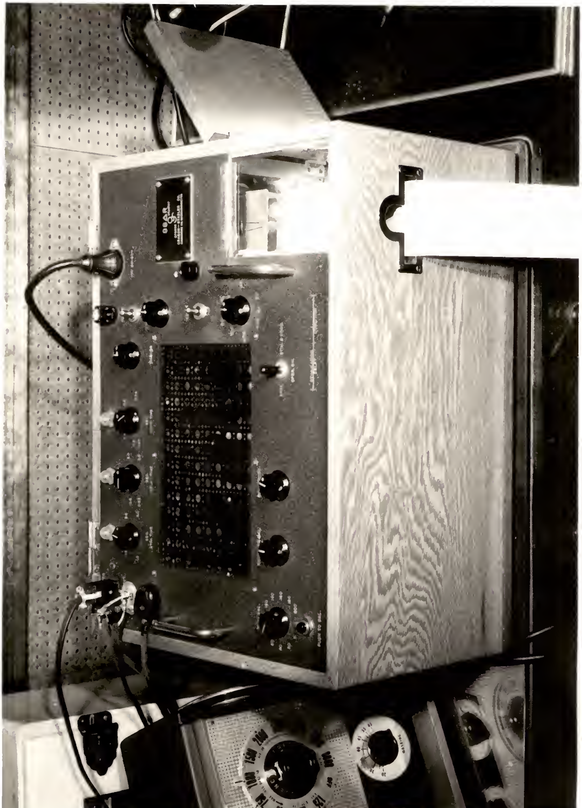

PLATE IV

APPLYING THE ELECTRODES

The subject is seated in a comfortable armchair in the testing room. The electrodes are applied to the proximal joints of the first and third fingers of each hand and to the wrist of the left hand. A liberal amount of electrode jelly is used. The finger electrodes are held in place by means of adhesive tape and the wrist electrode by means of a rubber strap.

PLATE V

SUBJECT USING CHAIR ARM-RESTS

The subject is resting his hands on the arms of the chair. This technique is suitable for adults but is unsatisfactory for testing children. This view shows how the experimenter may observe the subject from the control room either directly through the window or indirectly through the mirror. The control room is kept dark so that the subject cannot see into it.

PLATE VI

SUBJECT USING WOODEN BOARD FOR ARM-REST

The subject is resting his arms and hands on a board which fits over the arms of the chair. The table-top effect which is achieved is more suitable for testing young children. Toys and games may be placed on the board as distracting devices. This view also shows how the subject may be observed directly or through the mirror.

PLATE VII

CONDUCTING THE TEST

The subject remains in full view of the experimenter throughout the test. Although this is not necessary for PGSR audiometry, it is usually considered desirable to observe the subject after he has received medication, even when there is little likelihood of any untoward reaction occurring.

PLATE VIII

SAMPLE RECORDINGS

These recordings were picked at random from the tracings of eight different subjects to demonstrate the typical type of record obtained with the Grason-Stadler Psychogalvanometer as used in this study.

<u>Code</u>

CS - Conditioned Stimulus (Tone)

UCS- Unconditioned Stimulus (Shock)

CR - Conditioned Response

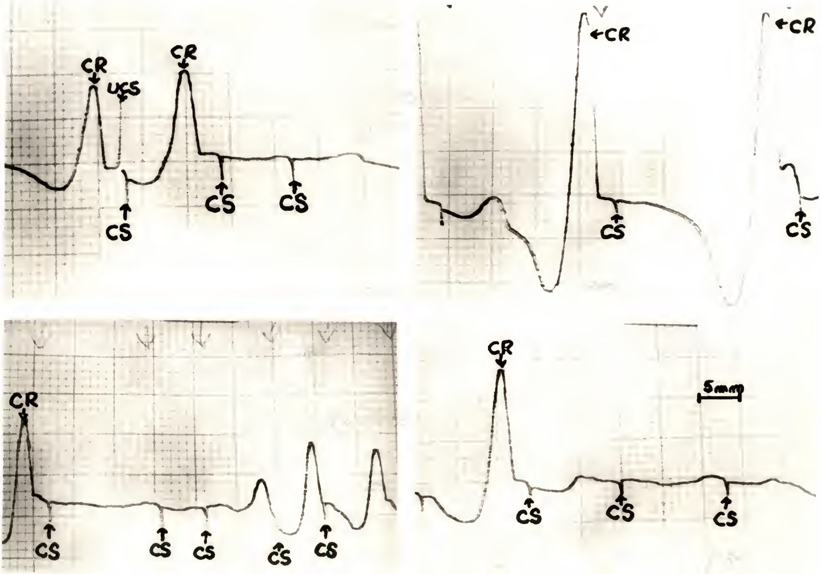
CR
UCS
CR
CS
CS
CS
CR
CR
CS
CS
CR
CS
CS
CS
CS
CS
CR
CS
CS
CS
5mm

PLATE VIII.--(Continued)

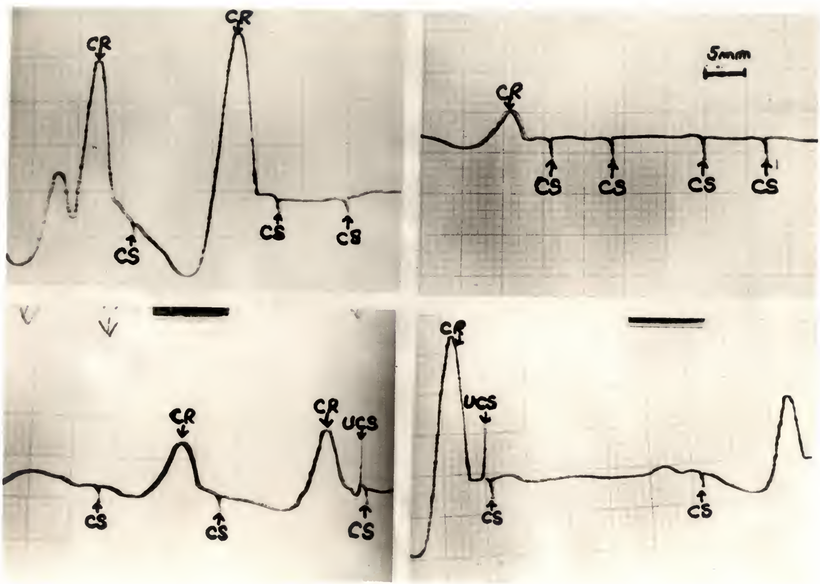
CR
CR
CS
CS
CS
5mm
CR
CS
CS
CS
CS
CR
CR
UCS
CS
CS
CS
CR
UCS
CS
CS

TABLE 7

LATIN SQUARE ARRANGEMENT FOR
COUNTERBALANCED ORDER

Subject	Order of Tests	Subject	Order of Tests
101	4 1 2 3	113	1 4 2 3
102	2 3 4 1	114	2 4 1 3
103	3 4 1 2	115	3 2 4 1
104	1 2 3 4	116	1 3 2 4
105	2 3 1 4	117	1 2 4 3
106	4 1 3 2	118	3 1 2 4
107	1 4 3 2	119	4 3 1 2
108	4 3 2 1	120	2 4 3 1
109	2 1 4 3	121	3 4 2 1
110	3 2 1 4	122	1 3 4 2
111	3 1 4 2	123	2 1 3 4
112	4 2 3 1	124	4 2 1 3

Test Number

1. PGSR -Placebo
2. PGSR -Tolseram
3. CA -Placebo
4. CA -Tolseram

TABLE 8

THRESHOLD VALUES FOR 500 CPS*

Subject	CA-T	CA-P	PGSR-T	PGSR-P	Σ_r	Σ^2_r
101	-10	-10	-10	-10	-40	400
102	- 5	- 5	- 5	- 5	-20	100
103	-10	-10	-10	-10	-40	400
104	-10	-10	-10	0	-30	300
105	-10	-10	-10	-10	-40	400
106	-10	- 5	-10	- 5	-30	250
107	-10	-15	-15	-10	-50	650
108	- 5	- 5	- 5	- 5	-20	100
109	-15	-15	- 5	- 5	-40	500
110	-10	- 5	- 5	- 5	-25	175
111	-10	-10	-10	-10	-40	400
112	-10	-10	-10	-10	-40	400
113	-10	-10	-10	- 5	-35	325
114	-10	-15	-15	-10	-50	650
115	-10	-10	-10	-10	-40	400
116	- 5	-10	- 5	-10	-30	250
117	-15	-10	-15	-15	-55	775
118	- 5	-10	-10	-10	-35	325
119	- 5	- 5	- 5	- 5	-20	100
120	-15	-15	-10	-10	-50	650
121	-10	-10	-10	-10	-40	400
122	-15	-15	-10	-10	-50	650
123	-10	-10	-10	-10	-40	400
124	-15	-15	-15	-10	-55	775
Σ_c	-240	-245	-230	-200	-915	
Σ^2_c	2650	2775	2450	1900		9775
Mean_c	-10.00	-10.21	-9.58	-8.33		

*Right ear

TABLE 9

THRESHOLD VALUES FOR 1,000 CPS*

Subject	CA-T	CA-P	PGSR-T	PGSR-P	Σ_r	Σ^2_r
101	-10	-10	-10	-10	-40	400
102	- 5	- 5	- 5	- 5	-20	100
103	-10	-10	-10	-10	-40	400
104	-10	-10	-10	-10	-40	400
105	- 5	-10	-10	-10	-35	325
106	-10	- 5	- 5	- 5	-25	175
107	-10	-10	-10	-10	-40	400
108	- 5	- 5	- 5	- 5	-20	100
109	-10	-10	- 5	-10	-35	325
110	-10	- 5	-10	- 5	-30	250
111	-10	- 5	- 5	-10	-30	250
112	-10	- 5	-10	- 5	-30	250
113	-15	-10	-15	-15	-55	775
114	-10	-10	-10	-10	-40	400
115	- 5	- 5	- 5	-10	-25	175
116	0	-10	-10	-15	-35	425
117	-10	-10	-10	-10	-40	400
118	- 5	-10	-10	-10	-35	325
119	- 5	- 5	- 5	-10	-25	175
120	- 5	- 5	- 5	-10	-25	175
121	- 5	0	0	0	- 5	25
122	-10	-10	-10	-10	-40	400
123	-10	-10	-10	-10	-40	400
124	-10	-10	-10	-10	-40	400
Σ_c	-195	-185	-195	-215	-790	
Σ^2_c	1825	1625	1825	2175		7450
Mean_c	-8.13	-7.71	-8.13	-8.96		

*Right ear

TABLE 10

THRESHOLD VALUES FOR 2,000 CPS*

Subject	CA-T	CA-P	PGSR-T	PGSR-P	$\sum_r$	$\sum^2_r$
101	-10	- 5	-10	-10	-35	325
102	- 5	-10	-10	- 5	-30	250
103	-10	-10	-10	-10	-40	400
104	-10	-10	-10	-10	-40	400
105	-10	-10	-10	-10	-40	400
106	+ 5	+ 5	+ 5	0	+15	75
107	-10	-10	-10	-10	-40	400
108	-10	- 5	-10	-10	-35	325
109	-10	-10	- 5	-10	-35	325
110	-10	- 5	-10	-10	-35	325
111	-10	- 5	-10	-10	-35	325
112	- 5	-10	-10	- 5	-30	250
113	- 5	-10	-15	-15	-45	575
114	-10	-10	-10	-10	-40	400
115	- 5	- 5	- 5	-10	-25	175
116	- 5	- 5	-10	-10	-30	250
117	- 5	-10	-10	-10	-35	325
118	- 5	0	- 5	- 5	-15	75
119	- 5	- 5	- 5	-10	-25	175
120	- 5	-10	- 5	-10	-30	250
121	-10	- 5	- 5	- 5	-25	175
122	0	- 5	- 5	-10	-20	150
123	-10	- 5	-10	- 5	-30	250
124	-10	-10	-10	-10	-40	400
$\sum_c$	-170	-165	-195	-210	-740	
$\sum^2_c$	1550	1475	1925	2050		7000
Mean_c	-7.08	-6.88	-8.13	-8.75		

*Right ear

TABLE 11

THRESHOLD VALUES FOR 4,000 CPS*

Subject	CA-T	CA-P	PGSR-T	PGSR-P	Σ_r	Σ^2_r
101	-10	-10	-10	-10	-40	400
102	-10	-10	-10	- 5	-35	325
103	-10	-10	-10	-10	-40	400
104	+20	+20	+20	+20	+80	1600
105	-10	-10	- 5	-10	-35	325
106	0	0	0	- 5	- 5	25
107	-10	-10	-10	-10	-40	400
108	0	0	0	0	0	0
109	-10	-15	-10	- 5	-40	450
110	-10	-10	-10	-10	-40	400
111	-10	-10	-15	-10	-45	525
112	+ 5	+ 5	+ 5	+ 5	+20	100
113	-10	-15	-10	-10	-45	525
114	0	+ 5	- 5	+ 5	+ 5	75
115	- 5	- 5	- 5	-10	-25	175
116	0	+ 5	0	-10	- 5	125
117	-10	- 5	- 5	- 5	-25	175
118	0	0	0	- 5	- 5	25
119	0	- 5	- 5	- 5	-15	75
120	+ 5	0	- 5	- 5	- 5	75
121	+ 5	+ 5	0	0	+10	50
122	0	+ 5	+ 5	0	+10	50
123	- 5	0	- 5	- 5	-15	75
124	- 5	- 5	- 5	0	-15	75
Σ_c	-80	-75	-95	-100	-350	
Σ^2_c	1550	1775	1575	1550		6450
Mean_c	-3.33	-3.13	-3.96	-4.17		

*Right ear

TABLE 12

THRESHOLD VALUES FOR 8,000 CPS*

Subject	CA-T	CA-P	PGSR-T	PGSR-P	Σ_r	Σ^2_r
101	-10	- 5	0	-10	-25	225
102	-10	-10	-10	-10	-40	400
103	-10	-10	-10	-10	-40	400
104	+15	+20	+20	+20	+75	1425
105	0	0	- 5	- 5	-10	50
106	+ 5	+ 5	+ 5	0	+15	75
107	- 5	-10	- 5	- 5	-25	175
108	0	- 5	- 5	0	-10	50
109	+15	+15	+15	+15	+60	900
110	- 5	- 5	- 5	- 5	-20	100
111	-10	-20	-10	- 5	-45	625
112	- 5	0	- 5	- 5	-15	75
113	0	-10	- 5	0	-15	125
114	0	+ 5	0	0	+ 5	25
115	- 5	-10	-10	-10	-35	325
116	+10	+20	+15	+20	+65	1125
117	-10	-15	-15	-10	-50	650
118	- 5	- 5	-10	- 5	-25	175
119	- 5	-10	-10	- 5	-30	250
120	0	0	0	0	0	0
121	- 5	-10	-10	-10	-35	325
122	+40	+40	+40	+40	+160	6400
123	0	0	0	0	0	0
124	-10	-10	-10	-10	-40	400
Σ_c	-10	-30	-30	-10	-80	
Σ^2_c	2950	4200	3650	3500		14300
$Mean_c$	-0.42	-1.25	-1.25	-0.42		

*Right ear

TABLE 13

BASAL LEVELS OF SKIN RESISTANCE IN KILO-OHMS

Subject Number	PGSR with Tolseram Beginning	End	PGSR with Placebo Beginning	End
101	40	20	60	40
102	180	60	60	40
103	80	65	40	20
104	80	60	80	60
105	70	60	180	120
106	100	60	100	60
107	20	10	80	60
108	120	80	40	40
109	80	60	60	40
110	80	60	80	60
111	60	40	60	40
112	80	60	60	80
113	20	30	120	40
114	40	20	80	100
115	80	80	40	40
116	30	30	80	20
117	60	50	60	40
118	30	20	40	20
119	30	20	30	20
120	60	60	40	40
121	30	20	20	20
122	40	10	40	40
123	40	40	40	20
124	30	20	40	20
Sum =	1480	1035	1530	1080
Mean =	61.67	43.13	63.75	45.00
S.D. =	38.03	22.16	34.24	26.87

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Raymond B. Strauss was born March 25, 1930 in New York, New York. He received his undergraduate education at the University of Oklahoma, Norman, Oklahoma and at Washington University, St. Louis, Missouri. He received the degree of Bachelor of Arts from the latter institution in September, 1950. He continued his studies in Speech at the Graduate School of Washington University and at the Central Institute for the Deaf, St. Louis, from September, 1950 to September, 1951.

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This dissertation was prepared under the direction of the chairman of the candidate's supervisory committee and has been approved by all members of that committee. It was submitted to the Dean of the College of Arts and Sciences and to the Graduate Council, and was approved as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

August 11, 1956

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